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Remarks

Applicant would like to thank the Examiner for the telephonic interview of May 25, 2004, with applicant's attorneys, Robert N. Young and Kathryn E. Cox, in which all of the current rejections in the present case were discussed. During the interview, the Examiner and applicant's attorneys came to a general agreement regarding the basis of the new paragraphs being added to the specification originating in Examples 1-4 of the provisional application. The Examiner and applicant's attorneys also reached a general agreement concerning the substance of claim amendments that may overcome the rejections based on a teaching by Van Ness et al. of the spacer configurations of the present invention.

Claims 22-39 are currently pending in the present application. Claim 22, claim 32, and claim 38 have been amended without prejudice in order to advance to the prosecution of the present application. The amendments to the claims are supported by the application as originally filed, do not add new matter, and are otherwise proper. Support for the amendment to claim 22 can be found throughout the application as originally filed, including without limitation paragraph [0068] through paragraph [0070]. Support for the amendments to claim 32 and claim 38 can also be found throughout the application as originally filed. Specific support for the amendments to claim 32 and claim 38 can be found in newly added paragraph [0074.15]. Applicant respectfully requests entry of these Amendments in their entirety.

These amendments change claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, are presented, with an appropriate defined status identifier. Because the amendments make explicit what was inherent, broaden or do not narrow the scope of the claim 22, claim 32, or claim 38, the claim amendments are not narrowing and the claims are entitled to the same scope either literally or under the Doctrine of Equivalents.

Applicant thanks the Examiner for indicating that the information disclosure statement submitted April 21, 2003 was considered in the present application. Applicant also thanks the Examiner for accepting the amendments to the drawings, the amendments to paragraphs [0052], [0072], [0068], [0069] and [0073], and the amendments of claim 22-32 in regards to the 35 U.S.C. § 112 rejections.

In view of the above amendments and following remarks, applicant respectfully requests reconsideration of the claims and submits that the application is in condition for allowance.

I. Amendment to the Specification

In the Office Action, the Examiner objected to the addition of paragraphs [0074.1] – [0074.18] into the specification as adding new matter. Applicant respectfully traverses. The paragraphs being added come directly from the provisional application on which this utility application is based. Paragraphs [0074.1] – [0074.18] can be found in the description of Examples 1-4 of the provisional patent application. Because the provisional patent application was wholly incorporated by reference in paragraph [0017], applicant respectfully submits that entry of the new paragraphs into the specification of the utility application is proper and requests the Examiner allow the entry.

Regarding the other information incorporated by reference in the patent application, and specifically the material incorporated by reference from Current Protocols in Molecular Biology (Ausubel et al.), all remaining information incorporated by reference is believed to be non-essential at this time. However, applicant reserves the right to amend the present application to include any material incorporated by reference that is considered to be essential.

II. Claim Interpretation

Applicant agrees to the Examiner's interpretation of the meaning of the phrase "wherein the oligonucleotides that are coupled to different bead sets are oligonucleotides with and without a spacer" to mean that "all combinations of oligonucleotides with and without spacers coupled to bead sets are permissible in the claimed invention so long as the claimed methods can be effectively performed.

Applicant disagrees with the Examiner's statement that random bases may include "any bases." Using the Examiner's definition would render the claimed methods inoperable. As used in the invention, the random bases of the spacer may include all bases except those bases that are complementary to the target oligonucleotide 5' or 3' of where the oligonucleotide

hybridizes with the target oligonucleotide. Thus, the random bases of the spacer may include all bases so long as the claimed methods can be effectively performed.

III. Claim Rejections

A. 35 U.S.C. §102(e)

In the Office Action, claims 22-29 and 31-38 were rejected under 35 U.S.C. § 102(e) as being anticipated by Van Ness et al. (U.S. Patent No. 6,361,940). Applicant respectfully traverses. Van Ness et al. cannot anticipate any of the present claims because Van Ness et al. fail to teach or suggest every element of the present claims. Specifically, Van Ness et al. cannot anticipate the present claims because they do not teach the spacer of the presently claimed methods. In amended claim 22, the “complementary regions of the oligonucleotides flank the spacer [and the] complementary regions of the oligonucleotides hybridize with a contiguous sequence on the target oligonucleotide.” Thus, the spacer of the present claims is located internally to an oligonucleotide sequence that is generally complementary to a target oligonucleotide and does not replace any of the bases in the oligonucleotide sequence. As such, the present spacer only lengthens the size of the molecule by separating two portions of a single oligonucleotide probe sequence complementary to a contiguous sequence on the target oligonucleotide. The nucleotide residues on the ends of the complementary sequence flanking the spacer become adjacent to each other when the oligonucleotide hybridizes with a target oligonucleotide.

In contrast, the “specificity spacer” in Van Ness et al. replaces a portion of an oligonucleotide complementary to a target sequence. Van Ness et al. clearly state “the base analog replaces a G, C, or T base in a probe or primer” and “base analogs... maintain essentially the ‘natural’ separation between adjacent nucleotides [and] have a moiety with approximately the same spatial requirements of a G, C, A, or T base.” Column 43, lines 46-47 and lines 34-38, respectively. See also, the sequence listing which states “N is an unnatural nucleotide (i.e., a nucleotide having a chemical moiety which is not one of A,G,C,T or U at the position normally occupied by A,G,C,T or U) or a molecular spacer that provides an equal linear distance, as a natural nucleotide, along the DNA phosphate sugar backbone.” Accordingly, the nucleotide residues that are adjacent to the ends

of the specificity spacer are separated from each other by the length of the specificity spacer when the oligonucleotide hybridizes with a target.

Furthermore, the specificity spacer of Van Ness et al. cannot encompass an additional 20 “bases” in the middle of a complementary oligonucleotide sequence. As acknowledged in the Office Action, Van Ness et al. teach a specificity spacer having a chain of 2-5 carbons. Col. 40, line 54. Because Van Ness et al. demonstrate two of these five carbons bonding together to form a 5-6 membered ring base analog, by definition only two base analogs are capable of forming using five carbons. Col. 41, line 10. Van Ness et al. further teach that the specificity spacers cannot be adjacent to each other. Col. 41, line 42. Therefore, a specificity spacer in Van Ness can only provide two base analogs and cannot be 20 “bases” long.

Accordingly, Van Ness et al. fail to teach or suggest all of the elements of independent claim 22 and applicant respectfully requests the Examiner withdraw this rejection.

Concerning the rejection of claims 23, 24-26, 27, 28, 29, 31, 32, 33-34, 35, 36, and 37-38 as anticipated by Van Ness et al., applicant respectfully traverses. Because Van Ness et al. do not teach or suggest all of the elements of the independent claim, Van Ness et al. cannot teach or suggest all of the elements of the claims that depend from that independent claim. For the foregoing reason, applicant respectfully requests the Examiner withdraw the anticipation rejection to claims 23, 24-26, 27, 28, 29, 31, 32, 33-34, 35, 36, and 37-38.

Furthermore, regarding claims 32 and 38 as amended, Van Ness et al. fail to teach or suggest any assay using beads labeled with fluorescent ratios. Although the Office Action stated that “Van Ness et al. teach oligonucleotides... coupled to different bead sets labeled with fluorescent labels such as BODIPY, TAMRA or Texas Red... (col. 83, lines 10-67),” Van Ness et al. make it clear in the cited example that the probe oligonucleotides, not the solid bead, is fluorescently labeled when they state “[e]ach probe oligonucleotide is labeled with either BODIPY, TAMRA or Texas Red.” Column 83, 29-30 (emphasis added). In fact, the fluorescently labeled probe oligonucleotide is not even immobilized on the solid support because only the “‘target’ oligonucleotide was immobilized on a set of solid supports.” Column 83, lines 19-21 (parenthetical omitted). Accordingly, the fluorescent label stays with the probe oligonucleotide and not the solid support, which Van Ness et al. make clear when they state that the probe oligonucleotide was denatured and the “solution [containing the denatured, labeled probe] is removed from the incubation tubes and

placed in a black microtiter plate. The plates are then read directly...” Column 83, lines 38-45 (parentheticals omitted). Van Ness et al. also cannot anticipate claims 32 or 38 because they further fail to teach or suggest bead sets that have a fluorescence color ratio. Because a ratio is a comparison between two different things, in order to have a fluorescence color *ratio*, the beads of claims 32 or 38 are labeled with at least two different fluorescent labels. Nowhere do Van Ness et al. teach a fluorescently labeled bead, much less a bead with at least two fluorescent labels. Accordingly, Van Ness et al. cannot anticipate dependent claims 32 and 38 because Van Ness et al. both fail to teach or suggest all of the elements of independent claim 22 from which claims 32 and 38 depend and Van Ness et al. fail to teach or suggest beads having a fluorescent ratio. Therefore, even if Van Ness et al. anticipated the independent claim from which claims 32 and 38 depend, which they do not, Van Ness et al. could not anticipate these claims as amended. Thus, applicant respectfully requests the Examiner withdraw the rejection and allow the claims to issue.

Also, regarding claim 33 and claim 34, the Office Action states that Van Ness et al. teach the spacer as being a nucleic acid base. However, Van Ness never discloses the use of a nucleic acid base as the spacer. As shown in the dictionary definition, a nucleic acid is “any of various acids (as DNA or RNA) that are composed of nucleotide chains.” (Merriam Webster’s Collegiate Dictionary, 10th ed. 1997). A nucleotide can be defined as “any of several compounds that consist of a ribose or deoxyribose sugar joined to a purine or pyrimidine base and to a phosphate group and that are the basic structural units of nucleic acids (as RNA and DNA).” *Id.* Van Ness et al. do not teach or suggest the use of a nucleic acid base as the spacer, but instead teach the use of a spacer containing an abasic residue or a base analog (or both). A base analog may take up the same amount of space as a nucleic acid base but it is NOT a nucleic acid as defined by those having skill in the art. An analog is defined as “a chemical compound that is structurally similar to another but differs slightly in composition (as in the replacement of one atom by an atom of a different element or in the presence of a particular functional group).” *Id.* Thus, Van Ness et al. disclose the use of something similar but not the same as a nucleic acid base for use in the specificity spacer. Because Van Ness et al. do not teach a nucleic acid base for use in the spacer, they cannot anticipate claim 33 and claim 34 of the present invention. Therefore, applicant respectfully requests the rejection to claim 33 and claim 34 be withdrawn and the claims allowed to issue.

B. 35 U.S.C § 103

a. Claims 22-29 and 31-38

In the Office Action claims 22-29 and 31-38 were rejected as obvious over Kaneoka et al. and Van Ness et al. Applicant respectfully traverses. In order to “establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art.” MPEP §2143.03. Applicant agrees with the Examiner’s statement in the Office Action that it is a combination of references, not references taken individually, that render the claims obvious. However, as stated in § 2143 of the MPEP, “[t]he prior art reference (or references when combined) must teach or suggest all of the claim limitations.” (emphasis added). Based on this standard, the combination of Kaneoka et al. and Van Ness et al. cannot render the rejected claims prima facie obvious because this combination of references fails to teach or suggest the present spacer configuration, an element of all of the rejected claims. As stated above, Van Ness et al. do not teach or disclose the present spacer configuration. Nor do Kaneoka et al. overcome this deficiency as even the Examiner admits that “Kaneoka et al. do not teach oligonucleotides with and without spacers coupled to different bead sets.” Accordingly, the combination Kaneoka et al. and Van Ness et al. cannot state a proper prima facie case of obviousness and applicant respectfully requests the Examiner withdraw this rejection.

b. Claim 30

Claim 30 was rejected as obvious over Kaneoka et al. and Van Ness et al. further in view of Nolan et al. However, Nolan et al. cannot overcome the deficiencies of Kaneoka et al. or Van Ness et al. because they also fail to teach or suggest the claimed spacer arrangement. Accordingly applicant respectfully requests the Examiner withdraw this rejection and allow the claim to issue.

c. Claims 22-29 and 31-39

Claims 22-29 and 31-39 were rejected in the Office Action as obvious over Armstrong et al. and Van Ness et al. Applicant respectfully traverses this rejection. As discussed above, Van Ness et al. do not teach all of the elements of the present claims because Van Ness et al. do not teach the present spacer configuration. Armstrong et al. cannot overcome this

deficiency because, as admitted by the Examiner, Armstrong et al. "do not teach oligonucleotides with and without spacers." Furthermore, with respect to claims 32 and 38, Van Ness et al. do not teach bead sets having a fluorescent color ratio. Accordingly, this combination of references cannot render the rejected claims prima facie obvious. In light of this, applicant respectfully requests the Examiner withdraw the obviousness rejection to claims 22-29 and 31-39.

d. Claim 31

Claim 31 was rejected in the Office Action as obvious over Armstrong et al. and Van Ness et al. further in view of Long. Applicant respectfully traverses the rejection of claim 31. Neither Armstrong et al. nor Van Ness et al. teach or suggest the spacer configuration of claim 22 from which claim 31 depends. Therefore, Armstrong et al. and Van Ness et al. cannot teach each and every element of the rejected claim. Long does not overcome this deficiency because it also fails to teach or suggest a spacer as presently claimed. Accordingly, applicant respectfully requests the Examiner withdraw this rejection and allow claim 31 to issue.

CONCLUSION

In view of the above remarks, it is respectfully submitted that this application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to telephone the undersigned at the number listed below if the Examiner believes such would be helpful in advancing the application to issue.

Respectfully submitted,

Date July 19, 2004

By

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181920RMcN97

anaconda

\y\ yet \zh\ vision \ä, ɛ, ɐ, œ, ʊ, ʉ, ʏ see Guide to Pronunciation

|ə| abut |ʔ| kitten, F table |ər| further |ə| ash |ā| acc |ā| mop, mar
 |ū| out |ch| chin |e| bet |ē| easy |g| go |ī| hit |ī| ice |ī| job
 |j| sing |ō| go |o| law |oi| boy |th| thin |th| the |ū| loot |ū| foot
 |y| yet |zh| vision |ä, ē, °, æ, ue, ū, see Guide to Pronunciation

tant point or indicate a transition (as of ideas) 4: SOMETIMES (~ one and ~ another) 5: under the present circumstances 6: at the time referred to (~ the trouble began)

now conj (bef. 12c): in view of the fact that: SINCE — often followed by that (~ that we are here)

now n (12c): the present time or moment (been ill up to ~)

now adj (14c): 1: of or relating to the present time: EXISTING (the ~ president) 2: a: excitingly new (~ clothes) b: constantly aware of what is new (~ people) (the ~ generation)

NOW account \ˈnau- or no-ways\ (negotiable order of withdrawal) (1974): a savings account on which checks may be drawn

now-a-days \ˈnau-(ə)-dāz\ *adv* [ME *now a dayes*, fr. *now* + *a dayes* during the day] (14c): at the present time

now and then adv (15c): from time to time: OCCASIONALLY (*now and then* we go off to the country)

no-way adv (13c) 1 \ˈnō-wā\ or *no-ways* \-wāz\ : NOWISE 2 *usu* *no way* \-wā\ : NO — used emphatically

no-where \ˈnō-hwēr-, -hwār-, -hwor or without h\ *adv* (bef. 12c) 1: not in or at any place 2: to no place

nowhere n (1831) 1: a nonexistent place 2: an unknown, distant, or obscure place or state (rose to fame out of ~) — *miles from nowhere*: in an extremely remote place

nowhere near adv (15c): not nearly

no-where \ˈnō-hwēr-, -hwār-, -hwor or without h\ *adv* (ca. 1866) chiefly dial: NOWHERE

no-whither \ˈnō-hwi-thər-, -wi-thər; nō-*adv* (bef. 12c): to or toward no place

no-win \ˈnō-wīn-, -wīn\ *adj* (1962): not likely to give victory, success, or satisfaction: that cannot be won (a ~ situation) (a ~ war)

no-wise \ˈnō-wīz\ *adv* (14c): not at all

now-ness \ˈnau-nəs\ *n* (1674): the quality or state of existing or occurring in or belonging to the present time

nowt \ˈnaut also ˈnōt\ *dial Eng var* of NOUGHT

nox-i-ous \ˈnäk-shəs\ *adj* [ME *noxius*, fr. L. *nox* harm; akin to L. *nocere* to harm, *ne-*, *ne-* violent death, Gk *nekros* dead body] (15c) 1: a: physically harmful or destructive to living beings (~ wastes that poison our streams) b: constituting a harmful influence on mind or behavior: morally corrupting (~ doctrines) 2: DISTASTEFUL OBNOXIOUS *syn* see PERNICIOUS — *nox-i-ous-ly adv* — *nox-i-ous-ness n*

noz-zle \ˈnā-zəl\ *n* [dim. of *nose*] (1683) 1: a projecting vent of something 2: a short tube with a taper or constriction used (as on a hose) to speed up or direct a flow of fluid, c: a part in a rocket engine that accelerates the exhaust gases from the combustion chamber to a high velocity 2 *slang*: NOSE

NSAID \ˈen-sed also -sād\ *n* [nonsteroidal anti-inflammatory drug] (1985): a nonsteroidal anti-inflammatory drug (as ibuprofen)

-n't vb comb form: not (isn't)

nth \ˈen(t)h\ *adj* [n (indefinite number) + -th] (1852) 1: numbered with an unspecified or indefinitely large ordinal number (for the ~ time) 2: EXTREME, UTMOST (to the ~ degree)

n-type \ˈen-ˈtīp\ *adj* [negative + type] (1946): relating to or being a semiconductor in which charge is carried by electrons — compare P-TYPE

nu \ˈnu-, nyū\ *n* [Gk *ny*, of Sem origin; akin to Heb *nūn* nun] (ca. 1823): the 13th letter of the Greek alphabet — see ALPHABET table

nu-ance \ˈnu-ˈän(t)s-, ˈnyū-, -ās; nū-, nyū-\ *n* [F, fr. MF, shade of color, fr. *nuer* to make shades of color, fr. *nue* cloud, fr. L *nubes*; perh. akin to W *nudd* mist] (1781) 1: a subtle distinction or variation 2: a subtle quality: NICETY 3: sensibility, awareness, or ability to express delicate shadings (as of meaning, feeling, or value) — *nu-anced* \-än(t)st-, -än(t)st\ *adj*

nub \ˈnʌb\ *n* [alter. of E dial. *knub*, prob. fr. LG *knubbe*] (1727) 1: KNOB, LUMP 2: NUBBIN 3: GIST, POINT

nub-bin \ˈnʌ-bən\ *n* [perh. dim. of *nub*] (1692) 1: something (as an ear of Indian corn) that is small for its kind, stunted, undeveloped, or imperfect 2: a small *usu*, projecting part or bit 3: NUB 3

nub-ble \ˈnʌ-bəl\ *n* [dim. of *nub*] (1818): a small knob or lump — *nub-bly* \-b(ə)-lē\ *adj*

nub-bly \-b(ə)-lē\ *adj* *nub-bi-er*, -est [nub + -i-er] (ca. 1876) 1: having or being like nubbles 2: having nubs (a ~ knit fabric)

Nu-bi-an \ˈnu-bē-ən-, ˈnyū-\ *n* (15c) 1: a native or inhabitant of Nubia 2: a member of one of the group of dark-skinned peoples that formed a powerful empire between Egypt and Ethiopia from the 6th to the 14th centuries 2: any of several languages spoken in central and northern Sudan — *Nubian adj*

nu-bile \ˈnu-bīl-, ˈnyū-, -bəl\ *adj* [F, fr. L *nubilis*, fr. *nubere* to marry — more at NUPIAL] (ca. 1642) 1: of marriageable condition or age 2: sexually attractive — used of a young woman — *nu-bil-i-ty* \ˈnyū-bī-lə-tē, ˈnyū-\ *n*

nu-cel-lus \ˈnu-ˈse-ləs-, ˈnyū-\ *n*, pl *nu-cel-li* \-ˈse-lī\ [NL, fr. L *nucella* small nut, fr. *nuc*, *nux* nut — more at NUT] (1882): the central and chief part of a plant ovule that encloses the female gametophyte — *nu-cel-lar* \-ˈse-lər\ *adj*

nu-chal \ˈnu-kəl-, ˈnyū-\ *adj* [ML *nucha* nape, fr. Ar *nukha* spinal marrow] (1835): of, relating to, or lying in the region of the nape

nucle- or **nucleo-** *comb form* [F *nucle*, *nucleo*, fr. NL *nucleus*] 1: nucleus (nucleoplasm) 2: nucleic acid (nucleoprotein)

nu-cle-ar \ˈnu-klē-ər-, ˈnyū-, -ˈkya-lər\ *adj* (1846) 1: of, relating to, or constituting a nucleus 2: a: of or relating to the atomic nucleus (~ reaction) (~ physics) b: used in or produced by a nuclear reac- (~ reaction) (~ fuel) (~ waste) (~ energy) c (1): being a tion (as fission) (~ nuclear power derives from an uncontrolled nuclear weapon whose destructive power derives from an uncontrolled nuclear reaction) (2): of, produced by, or involving nuclear weapons (the ~ reaction) (3): armed with nuclear weapons (~ powers) d: of, age) (~ war) or, powered by nuclear energy (a ~ submarine) (the ~ debate) (a ~ plant)

usage Though disapproved of by many, pronunciations ending in \-kya-lər\ have been found in widespread use among educated speakers including scientists, lawyers, professors, congressmen, U.S. cabinet members, and at least one U.S. president and one vice president. While most common in the U.S., these pronunciations have also been heard from British and Canadian speakers.

nuclear family n (1947): a family group that consists only of father, mother, and children

nuclear magnetic resonance n (1942): the magnetic resonance of atomic nucleus

nuclear medicine n (1952): a branch of medicine dealing with the use of radioactive materials in the diagnosis and treatment of disease

nuclear membrane n (1888): a double membrane enclosing the nucleus and having its outer part continuous with the endoplasmic reticulum — see CELL illustration

nuclear-powered adj (1948): powered by nuclear energy

nuclear resonance n (1940): the resonance absorption of a gamma ray by a nucleus identical to the nucleus that emitted the gamma ray

nuclear sap n (1877): the clear homogeneous ground substance of a cell nucleus — called also *karyolymph*

nuclear winter n (1983): the chilling of climate that is hypothesized to be a consequence of nuclear war and to result from the global blockage of sunlight by high-altitude dust clouds produced by nuclear explosions

nu-cle-ase \ˈnu-klē-ās-, ˈnyū-, -āz\ *n* (1902): any of various enzymes that promote hydrolysis of nucleic acids

nu-cle-ate \ˈnu-klē-āt-, ˈnyū-\ *vb* -at-ed, -at-ing [LL *nucleatus* nucleated to become stony, fr. L *nucleus*] vi (ca. 1864) 1: to form a nucleus: CLUSTER 2: to act as a nucleus for 3: to supply nuclei ~ vi 1: to form a nucleus 2: to act as a nucleus 3: to form ~ *nu-cle-ation* \ˈnu-klē-ā-shən-, ˈnyū-\ *n* — *nu-cle-ate* \ˈnu-klē-āt-, ˈnyū-\ *n*

nu-cle-at-ed \ˈnu-klē-ā-təd-, ˈnyū-\ or *nu-cle-ate* \ˈnu-klē-āt\ *adj* [NL, fr. *nucleatus*, fr. *nucleus* kernel] (1845) 1: having a nucleus or nuclei (a ~ cell) 2 *usu* *nucleate*: originating or occurring at nuclei (a ~ cell) boiling

nu-cle-ic acid \ˈnu-klē-ik-, -klā-, ˈnyū-\ *n* [fr. their occurrence in nucleic acids] (1892): any of various acids (as DNA or RNA) that are composed of nucleotide chains

nu-cle-in \ˈnu-klē-ən-, ˈnyū-\ *n* (1878) 1: NUCLEOPROTEIN 2: NUCLEIC ACID

nu-cle-o-cap-sid \ˈnu-klē-ə-ˈkəp-səd-, ˈnyū-\ *n* (1963): the nucleocapsid and surrounding protein coat in a virus

nu-cle-oid \ˈnu-klē-ōid-, ˈnyū-\ *n* (1938): the DNA-containing structure of a prokaryotic cell (as a bacterium)

nu-cle-o-lus \ˈnu-klē-ə-ləs-, ˈnyū-\ *n*, pl *-li* \-lī\ [NL, fr. L dim. of *nucleus*] (1845): a spherical body of the nucleus of most eukaryotic cells; becomes enlarged during protein synthesis, is associated with a nucleolus organizer, and contains the DNA templates for ribosomal RNA — see CELL illustration — *nu-cle-o-lar* \-lər\ *adj*

nucleolus organizer n (1939): the specific part of a chromosome with which a nucleolus is associated esp. during its reorganization

nuclear division — called also *nucleolar organizer*

nu-cle-on \ˈnu-klē-ən-, ˈnyū-\ *n* [ISV] (1923) 1: a nuclear particle: PROTON 2: NEUTRON 2: a hypothetical single entity with one unit of isospin that can manifest itself as either a proton or a neutron

nu-cle-on-ic \ˈnu-klē-ə-nik-, ˈnyū-\ *adj* *nu-cle-on-ics* \-ˈnīks-, ˈnyū-\ *n* pl *but sing or pl in constr* (1892): a branch of physical science that deals with nucleons or with all the phenomena of the atomic nucleus

nu-cle-o-phil \ˈnu-klē-ə-fīl-, ˈnyū-\ *n* (1943): a nucleophilic substance (as an electron-donating reagent)

nu-cle-o-phil-ic \ˈnu-klē-ə-fī-līk-, ˈnyū-\ *adj* (1933) 1: of an atom, molecule, or group: having an affinity for atomic nucleus: being an electron donor 2: involving a nucleophilic species (a ~ reaction) — compare ELECTROPHILIC — *nu-cle-o-phil-i-cal-ly* \-lī-k(ə)-lē\ *adv* — *nu-cle-o-phil-i-ty* \-lī-k(ə)-lī-tē\ *n*

nu-cle-o-plasm \ˈnu-klē-ə-plā-zəm-, ˈnyū-\ *n* [ISV] (1888): the plasma of a nucleus; esp.: NUCLEAR SAP — *nu-cle-o-plas-mic* \-ˈplāz-mīk\ *adj*

nu-cle-o-pro-tein \ˈnu-klē-ə-ˈprō-tēn-, ˈnyū-, -ˈprō-tē-ən\ *n* (1907): a compound that consists of a protein (as a histone) conjugated with a nucleic acid (as a DNA) and that is the principal component of the hereditary material in chromosomes

nu-cle-o-side \ˈnu-klē-ə-sīd-, ˈnyū-\ *n* [ISV *nucle-* + *-ose* + *-side*] (1911): a compound (as guanosine or adenosine) that consists of a purine or pyrimidine base combined with deoxyribose or ribose — found esp. in DNA or RNA

nu-cle-o-some \-sōm-, ˈnyū-\ *n* (1962): any of the repeating globular units of chromatin that consist of a complex of DNA and histone

nu-cle-o-somal \ˈnu-klē-ə-sō-məl-, ˈnyū-\ *adj*

nu-cle-o-syn-the-sis \ˈnu-klē-ə-sīn(t)-thə-səs-, ˈnyū-\ *n* [NL] (1892): the production of a chemical element from simpler nuclei (as of hydrogen) esp. in a star — *nu-cle-o-syn-thet-ic* \-sīn(t)-thē-tīk\ *adj*

nu-cle-o-tid-ase \ˈnu-klē-ə-tī-dās-, ˈnyū-, -dāz\ *n* (1911): a phosphatase that promotes hydrolysis of a nucleotide (as into a nucleoside and phosphoric acid)

nu-cle-o-tide \ˈnu-klē-ə-tīd-, ˈnyū-\ *n* [ISV, irreg. fr. *nucle-* + *-ide*] (1908): any of several compounds that consist of a ribose or deoxyribose sugar joined to a purine or pyrimidine base and to a phosphate group and that are the basic structural units of nucleic acids (as DNA) — compare NUCLEOSIDE

nu-cle-us \ˈnu-klē-əs-, ˈnyū-\ *n*, pl *nu-clei* \-klē-, ˈnyū-\ also *nu-cle-i* [NL, fr. L, kernel, dim. of *nuc*, *nux* nut — more at NUT] (1700): the small brighter and denser portion of a galaxy or of the head of a comet 2: a central point, group, or mass about which gathering, concentration, or accretion takes place: as a: a cellular organ or group of nerve cells in the central nervous system b: a mass of matter or group of nerve cells in the central nervous system c: a characteristic and stable complex of atoms or groups in a molecule d: the positively charged central part of an atom that comprises nearly all of the atomic mass and consists of protons and neutrons except in hydrogen which consists of a single proton only 3: the peak of sonority in the utterance of a syllable — *nu-clide* \ˈnu-kli-d-, ˈnyū-\ *n* [nucleus + Gk *eidōs* form, species — at IDOL] (1947): a species of atom characterized by the number of its nucleus and hence by the number of protons, the number of neutrons, and the energy content — *nu-clid-ic* \ˈnu-kli-dīk-, ˈnyū-\ *adj*

nude \ˈnüd-, ˈnyüd\ *adj* *nud-er*; *nud-est* [L *nudus* naked]